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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,146	12/10/2001	Jay Cunningham	3078/04	7806

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EXAMINER
SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,146	CUNNINGHAM ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,7,9 and 14-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7,9 and 14-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5-6-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Amendment filed April 1, 2005 is acknowledged. New claims 15-26 are presented. Accordingly, claims 1, 3, 5, 7, 9 and 14-26 are now under consideration.

An Information Disclosure Statement filed May 6, 2005 is further acknowledged and has been reviewed to the extent each reference is presented in the English language.

In the last Office Action the disclosure was objected to for the misspelling of "methotrexate" in claims 1, 5 and 9.

The objection is withdrawn following correction of the spelling.

Claims 1, 3, 5, 7 and 9-14 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-100 of copending Application No. 10/865414 in the last Office Action. Although the conflicting claims are not identical, they are not patentably distinct from each other because of overlapping subject matter.

Applicants have elected to hold this issue in abeyance. This obviousness-type double patenting rejection is maintained.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5, 7, 9 and 14-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-9, 13 and 23 of U.S. Patent No. 6,013,651. Although the conflicting claims are not identical, they are not patentably distinct from each other because the open language of the claims allows for the administration or addition of other active therapeutic agents. Combination therapy to inhibit melanoma or lung carcinoma is conventional.

Claims 1, 3, 5, 7, 9 and 14-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8-13 of copending Application No. 10/348274. Although the conflicting claims are not identical, they are not patentably distinct from each other because of overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, 5, 7 and 9-13 were rejected in the last Office Action under 35 U.S.C. 112, first paragraph, because, it was asserted, the specification does not reasonably provide enablement for preventing any neoplastic disease.

Following the most recent amendments to claims 1 and 5, the claims are directed to preventing or inhibiting melanoma growth, lung carcinoma growth or hypercalcemia comprising administering a compound of the formula of instant claims 1 and 5, together with one of fourteen recited chemotherapeutic agents, and pharmaceutical compositions

thereto, claim 9. The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to prevent the growth of melanoma or lung carcinoma without resorting to undue experimentation. Further, the specification only provides support for hypercalcemia in the condition of "humoral hypercalcemia of malignancy", not any hypercalcemic disorder. The specification provides support for showing an additive effect following the administration of compound XII with cyclophosphamide or cisplatin to treat two distinct tumor cell lines, the M21 human melanoma model and the LLC tumor, respectively.

The rejection is repeated for the reasons of record and presently extended to include new claims 15-26.

The broad recitation "preventing or inhibiting... hypercalcemia" is inclusive of many pathologies that presently have no established successful therapies and lack adequate enablement by the specification. Claims directed solely to inhibiting melanoma growth, lung carcinoma growth or humoral hypercalcemia of malignancy would obviate the rejection.

In the last Office Action claims 1, 3, 5, 7 and 9-13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Ruminski et al., WO 97/08145, and Remington's Pharmaceutical Sciences. It was asserted Ruminski teaches compounds that differ from those presently claimed in the formula of instant claims 1, 5 and 9 by the position of one halide. See the second and third compounds on page 791 and the first and second compounds on page 792. The compounds are taught to be useful to treat and inhibit solid tumor growth. See page 12, lines 28-33. It would have been reasonable to

expect compounds of such close structural similarity, i.e., as position isomers, to demonstrate the same ability to antagonize integrin $\alpha_v\beta_3$ and exhibit anti-solid tumor growth properties. Motivation to combine other active ingredients, and to prepare a pharmaceutical composition comprising the claimed compounds with other known antineoplastic agents, is provided on page 29, lines 22-23. Remington discloses two established anti-neoplastic agents, cyclophosphamide and fluorouracil.

Applicants argue results from monotherapies of the claimed compounds alone or the chemotherapeutic agents alone would not have provided motivation to a skilled artisan to use the recited combinations. Unexpected and additive benefits are disclosed by combination therapy on pages 106-107 of the specification for inhibiting the growth of a melanoma cell line and a lung carcinoma cell line.

Applicants' arguments are persuasive. Accordingly, the rejection of record under 35 U.S.C. 103 is withdrawn.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached Mondays to Fridays from 10:30 AM to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Chris Low, can be reached at telephone number 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

June 24, 2005